Amendments to the Specification

The paragraph which appears at page 2, lines 4 to 6, has been amended to read as follows.

Cross-reference to Related Application: This application is a division of U.S. Application No. 09/358,036, filed on July 21, 1999, which is a continuation-in-part of U.S. Patent application Serial No. 09/097,239, filed on June 12, 1998, the contents of the entirety of both applications ~~which~~ are hereby incorporated by ~~this~~ reference.

The paragraph which appears at page 7, lines 15 to 18, of the specification has been amended as follows:

FIG.5: Construction of pIG.NEO. pIG.NEO contains the Neo^R operatively linked to the E1B promoter. pIG.NEO was constructed by ligating the *HpaI-ScaI* fragment of pAT.PCR2.NEO.p(A) or pIG.E1A.NEO which contains the E1B promoter and Neo^R into the *EcoRV-ScaI* sites of pBS.

The paragraph which appears at page 13, lines 17 to 18, of the specification has been amended as follows:

FIG. 36 (A ~~I~~ and B ~~H~~) (Example 20): Schematic overview of constructing an arrayed adenoviral cDNA expression library.

The paragraph which appears at page 13, lines 19 to 24, of the specification has been amended as follows:

FIG. 37 (A, B, C, and D) (Example 21): Comparison of cotransfections of different adapter plasmids and pWE/Ad.AflII-rITRDE2A on 384-well plates with cotransfections on 96-well plates. The percentage of virus producing wells (CPE positive wells) scored at different time points as indicated after propagation of the

freeze/thawed transfected cells to new PER.C6/E2A cells 5 days after transfection (upper panel) or 7 days after transfection (lower panel) is shown.

The paragraph which bridges page 13, line 30 to page 14, line 4, of the specification has been amended as follows:

FIG. 39 (A, B, and C) (Example 23): The percentage of virus producing cells (CPE positive) scored after propagation of the freeze/thawed transfected cells to new PER.C6/E2A cells, in three different experiments using PER.C6/E2A cells for transfections with indicated confluency at time of transfection. The figure legend refers to Table 9 where the absolute cell numbers from each flask in each experiment were counted. The cells from these flasks were used to seed 96-well plates for transfection with adenoviral adapter and helper DNA molecules.

The paragraph which bridges page 40, line 31 to page 41, line 5, of the specification has been amended as follows:

This construct is of use when established cells are transfected with E1A.E1B constructs and NEO selection is required. Because NEO expression is directed by the E1B promoter, NEO resistant cells are expected to co-express E1A, which also is advantageous for maintaining high levels of expression of E1A during long-term culture of the cells. pIG.NEO was generated by cloning the *HpaI-ScaI* fragment of pAT.PCR2.NEO.p(A) or pIG.E1A.NEO, containing the NEO gene under the control of the Ad5 E1B promoter into pBS digested with *EcoRV* and *ScaI*.

The paragraph which bridges page 99, line 28 to page 100, line 3, of the specification has been amended as follows:

In FIG.36A and FIG. 36B, an overview is given of the scheme of an adenoviral cDNA expression library constructed and arrayed as described above.

This scheme describes the construction of libraries of individually cloned adenoviral vector libraries in a high throughput fashion. The improvement of this strategy over pooled libraries is that no bias for viruses with a growth advantage can occur. This is because individual members of the library are in the format of individual colonies straight after the plating of the library, and are kept individually during all further procedures.

The paragraph that bridges page 100, line 24, to page 101, line 12 of the specification has been amended as follows:

Essentially, this experiment was performed as described in Example 10, except for the following minor changes. The day before transfection, PER.C6/E2A cells were diluted with culture medium (DMEM with 10% fetal bovine serum and 10 mM $MgCl_2$) to a suspension of 11,250 cells per 25 μl, followed by seeding 25 μl per well of a 384-well tissue culture plate using a 16 channel multichannel pipette (Finn). After adding 1.3 ml serum free DMEM to the DNA/lipofectamine mixture, 15 μl of this mixture was then added to each PER.C6/E2A seeded well that had been washed with 25 μl DMEM prior to transfection. After 3 hours in a humidified CO_2 incubator (39°C, 10% CO_2), 50 μl culture medium was added to each well and the plates were returned to the humidified CO_2 incubator (39°C, 10% CO_2). The next day, the medium of each well was replaced with 50 μl culture medium. The plates were then returned to a humidified CO_2 incubator (32°C, 10% CO_2) for an additional 4 days, after which the wells were subjected to freezing at -20°C overnight followed by thawing and resuspension by repeated pipetting. An aliquot of 25 μl of the freeze/thawed transfected cells was transferred to each well of a plate with fresh PER.C6/E2A cells seeded as described above on 384-well tissue culture plates (plate 2). The second 384-well plate, with PER.C6/E2A cells incubated and thus infected with freeze/thawed cell lysate of the first transfected plate, was

checked for CPE formation and stored at -20°C. The experiment mentioned above was performed twice. In FIG. 37A, FIG. 37B, FIG. 37C, and FIG. 37D, the percentage of CPE positive wells scored after propagation of the freeze/thawed transfected cells to new PER.C6/E2A cells is depicted.

The paragraph which appears at page 104, lines 3 to 16, in the specification have been amended as follows:

The second plate of the two transfected plates was used for virus production. Seven days after transfection, the wells of the second plate were subjected to freezing at -20°C overnight, followed by thawing and resuspension by repeated pipetting. A 100 μl aliquot of the freeze/thawed transfected cells was transferred to each well of a plate with new PER.C6/E2A cells ($2.25x10^4$ cells per well in 100 μl) that were seeded in 96-well tissue culture plates one day prior to infections. The plate was incubated in the humidified CO_2 incubator (32 °, 10% CO_2) until the presence of full CPE was observed. In FIG. 39A, FIG. 39B, and FIG. 39C, the percentage of virus producing cells (CPE positive) wells), scored after propagation of the freeze/thawed transfected cells to new PER.C6/E2A cells, is depicted.

The data indicate that the level of confluency of the PER.C6/E2A cells, prior to transfection with the adenoviral adapter and helper DNA molecules, influences the final percentage of virus producing wells. The higher confluency was the most optimal for absolute final number of wells producing virus and the speed at which the virus generation occurs.